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Community-Based Evaluation of CT-Derived Liver Attenuation Index and Morphological Features as Early Predictors of Metabolic Risk: Correlation with Serum Biomarkers Before and After Medical and Lifestyle Interventions

INTRODUCTION

• Non-alcoholic fatty liver disease (NAFLD) is a major cause of cirrhosis and hepatocellular carcinoma. NAFLD represents a hepatic pathology exhibiting strong associations with adiposity, impaired insulin sensitivity, dyslipidemia, and the constellation of metabolic derangements collectively termed metabolicsyndrome (1). NAFLD represents a continuum of liver pathologies, extending from steatosis with or without mild inflammatory changes to Non-alcoholic steatohepatitis (NASH), which is distinguished by necroinflammation and an increased rate of fibrosis progression relative to non-alcoholic fatty liver (1, 2) .

• The standard histopathological grading system, notwithstanding its established clinical value, presents several inherent limitations. In response to the escalating incidence of NAFLD and the acknowledged limitations of hepatic biopsy, non-invasive imaging techniques have undergone rapid development, offering the potential for dependable identification of hepatic steatosis (3) .

• Non-contrast CT, a prevalent imaging modality, provides a quantitative measure of hepatic adiposity through the Liver Attenuation Index (LAI) and allows for the detection of macroscopic liver changes, including hepatomegaly, caudate lobe hypertrophy, surface nodularity, splenomegaly, and dilation of the portal vein. The LAI, a parameter extracted from CT imaging, offers improved diagnostic capabilities for hepatic steatosis compared to traditional CT (4, 5) . While cross-sectional studies have examined LAI, there is a paucity of research elucidating the dynamic changes in LAI and hepatic-splenic morphology following metabolic intervention and their subsequent association with alterations in serum markers indicative of improvement. Prior work isolates biomarkers, missing synergistic risk stratification via combined CT (e.g., LAI, liver-spleen difference) and serum markers.

RATIONALE

• CT assesses hepatic attenuation, liver volume, and perihepatic fat, all linked to liver function. However, there's limited prospective data from India connecting CT-based hepatic morphometry with liver-specific biochemical markers (e.g.,ALT, GGT, lipid profiles) and variations due to lifestyle and pharmacological changes. This study aims to address this gap by examining CT-derived liver parameters and their relationship with liver biomarkers at baseline and two follow-ups after intervention in the general population, regardless of alcohol consumption history.

AIM

To evaluate the utility of dynamic CT-based assessment of LAI and morphological parameters in predicting and monitoring systemic inflammation and metabolic risk, through correlation with serum biomarkers before and after therapeutic intervention.

OBJECTIVES

1. To assess CT-derived liver attenuation index and morphological features as early, non-invasive indicators of metabolic risk in a community-based population.
2. To correlate these imaging parameters with key serum biomarkers.
3. To evaluate changes in liver attenuation and morphology following medical and lifestyle interventions.
4. To determine the relationship between imaging changes and improvements in metabolic biomarkers post-intervention.

REVIEW OF LITERATURE

• **Maurice & Manousou, 2018** (6) explain NAFDL, which is characterized by ≥5% macrovesicular steatosis in hepatocytes, excluding secondary etiologies like

alcohol or drugs. This spectrum ranges from NAFL to NASH, fibrosis, and cirrhosis. Despite being a leading cause of global chronic liver disease, public awareness remains low, and cirrhosis complications are often overlooked in obesity discussions. NAFLD research is rapidly advancing, promising therapeutic transformations.

• **Milić, Lulić, & Štimac, 2014** (7) , NAFLD, the most prevalent global hepatopathy, spans from simple steatosis to NASH. As a hepatic component of metabolic syndrome, NAFLD demonstrates a significant correlation with obesity, with visceral fat deposition playing a pivotal role. The resultant insulin resistance and consequent liver injury are mediated by elevated free fatty acid levels and the activation of inflammatory processes. Weight loss is the primary therapeutic approach.

• **Piazzolla & Mangia, 2020** (8) demonstrated the delayed clinical manifestation of NAFLD and NASH impedes timely intervention, highlighting the necessity for early detection methodologies. Despite liver biopsy's established role in diagnosis and prognosis, its invasiveness and associated risks necessitate the development of reliable, non-invasive biomarkers. Current non-invasive biomarkers exhibit limitations in accurately identifying steatosis, early NASH, and predicting disease trajectory, hindering effective management and treatment monitoring.

• **Chaudhary et al., 2021** (9) explain the LAI. The LAI is a CT-based measurement used to assess hepatic steatosis, which refers to fat accumulation in the liver. A LAI value of -10 HU or lower suggests moderate to severe hepatic steatosis.

• **Cucoranu et al., 2023** (10) conducted a quantitative analysis of 119 individuals with non-alcoholic fatty liver disease to establish the relationship between abdominal anthropometry and liver density, assessed via non-contrast CT. The

study demonstrated significant inverse correlations between liver attenuation and waist circumference, as well as subcutaneous fat thicknesses at specific abdominal sites. Furthermore, multivariate logistic regression identified waist circumference, subcutaneous fat measurements, type 2 diabetes status, and elevated GGT as independent risk factors for NAFLD.

• **Chung et al., 2021** (11) explored the correlation between the Hepatic Steatosis Index (HSI) and NAFLD diagnosed via non-contrast CT in an asymptomatic cohort. Analysis of abdominal CT scans, liver and spleen attenuation values were quantified by two radiologists to define hepatic steatosis (liver attenuation <;10 HU). Univariate and logistic regression analyses assessed the relationship between steatosis and clinical parameters, revealing significant associations with fasting glucose, triglycerides, ALT/AST ratio, BMI, and HIS, suggesting potential metabolic abnormalities.

• **Taydas & Koc, 2020** (12) aimed to determine the utility of unenhanced abdominal CT for detecting hepatic steatosis in an asymptomatic population. CT scans were analyzed using three quantitative criteria based on hepatic and splenic attenuation values. These imaging results were correlated with anthropometric measurements (organ sizes, abdominal dimensions, subcutaneous fat). The prevalence of steatosis varied (23.3%-67.1%) based on the diagnostic criteria applied.

MATERIALS AND METHODS

● **Study Area:** Shalinitai Meghe Hospital and Research Centre (SMHRC), Nagpur and Datta Meghe Medical college, Wanadongri, Nagpur (DMMC).

● **Source of Data:** Patients referring to the Department of Radiology.

● **Research design:** This is a prospective observational study with baselines and follow-ups at 3 and 6 months.

● **Duration of Study:** 2 years (2025 to 2027).

● **Subjects:** Patients referring to the Department of Radiology.

- **Sampling Procedure**: With informed consent duly acquired, a detailed patient history will be compiled. Subsequently, the patient will be assessed using Dynamic CT-Based methodology, specifically analyzing the liver attenuation index and morphological parameters, for the predictive and longitudinal evaluation of systemic inflammatory processes and metabolic risk.
- **Confidentiality:** The data collected will be kept confidential. The data will be coded and entered in the password-protected digital form. The names and other personal details of the patients will not be revealed.
- **Sample size:**

Using the Daniel Formula

• Where z 2 is the level of significance at 5% i.e. 95% confidence interval = 1.96

• Estimated prevalence= 50% (most conservative assumption) → P=0.5

• D= desired error of margin=5% = 0.05

The sample size was calculated to be 92 (10)

INCLUSION CRITERIA

 Adults aged 18 to 75 years residing in the community who are willing to participate

 Individuals undergoing non-contrast abdominal CT scans for routine health evaluation or non-hepatic indications

 Participants with at least one known metabolic risk factor

 Willingness to undergo medical and/or lifestyle interventions and attend follow-up assessments

EXCLUSION CRITERIA

 Chronic liver disease or liver cirrhosis

 Use of hepatotoxic medications or drugs known to affect liver fat independently

 Known malignancy or systemic illness

 Pregnancy or lactation

 Incomplete imaging or laboratory data at baseline or follow-up

- **Methodology**

CT Imaging Parameters

1. LAI:

Mean liver HU (three regions in right lobe) – mean spleen HU (three regions)

2. Liver and Spleen Morphology:

 Liver right lobe craniocaudal length

 Left and caudate lobe dimensions

 Liver surface (smooth / mildly nodular / markedly nodular)

 Portal vein diameter (before bifurcation)

 Spleen length and volume (splenic index)

Laboratory Parameters

 Liver enzymes: ALT, AST, ALP

Follow-Up

3- and 6-Months Participants will receive dietary and/or pharmacological intervention for metabolic syndrome.

Repeat non-contrast CT and blood investigations at 3 and 6 months.

Compare pre- and post-treatment changes in:

- LAI - Liver and spleen size
- Surface features and portal vein caliber
- Serum biomarkers

STATISTICAL ANALYSIS

All the statistical analyses will be carried out according to the Subjects, who will be

included in the research. Results will be presented for continuous variables as mean and SD or variables (numbers and percentages). Continuous variables that follow a normal distribution will be compared by a paired t-test of dependent samples or by the

Wilcoxon test if a normal distribution cannot be assumed. Categorical variables will be compared through the chi-square test. the outcome will be P-values less than 0.05

indicate that a significant.

SCOPE

This study focuses on evaluating CT-derived liver attenuation index (LAI) and

morphological features as early predictors of metabolic risk, assessing their correlation with serum biomarkers before and after medical and lifestyle interventions. It includes an analysis of liver attenuation, macroscopic features such as hepatomegaly and caudate lobe hypertrophy, and spleen-related changes. Additionally, biochemical correlations will be established between CT-derived parameters and liver biomarkers like ALT, AST, and lipid profiles, along with assessments of intervention-related changes at baseline, three months, and six months post-treatment. The study excludes individuals with chronic liver disease, those on hepatotoxic medications, and participants outside the age range of 18 to 75 years. Given its focus on non-contrast CT imaging, the study aims to enhance understanding of non-invasive imaging markers for metabolic health, contributing to early risk detection and personalized intervention strategies. Findings may support the integration of CT-based assessments into routine clinical

evaluation, bridging radiology and metabolic biomarker assessments to facilitate preventive healthcare approaches.

IMPLICATIONS

In the proposed study, CT-derived liver attenuation and morphological features will be evaluated as early predictors of metabolic risk, correlated with serum biomarkers before and after medical and lifestyle interventions. The results of this study could contribute to radiology's role in preventive medicine by identifying non-invasive imaging markers that reflect metabolic health and treatment response. If successful, it may help shift imaging from a diagnostic to a predictive tool, aiding in early detection and personalized intervention strategies.

The work provides practical experience in image analysis and data interpretation, as well as interdisciplinary research, enriching the knowledge of translational radiology and its relevance to health care. The study could contribute to the development of standardized radiological markers for metabolic risk, influencing future screening and management protocols. The research could improve early risk assessment as well as reduce the burden of metabolic diseases in a broader population through more targeted and timely interventions.

CONCLUSION

The potential of CT-based hepatic attenuation index (LAI) and structural characteristics as early predictors of metabolic risk will be elucidated in this study. A strong correlation will be examined between these imaging parameters and serum biochemical markers before and after medical and lifestyle interventions. By utilizing a non-invasive imaging approach, the research will aim to provide valuable insights into the dynamic alterations in hepatic parameters and their association with systemic metabolic changes. This will support the integration of CT assessments with conventional biochemical analyses, offering a more comprehensive method for evaluating hepatic steatosis and tracking the progression of metabolic syndrome. Ultimately, the findings will underscore the value of early detection and timely management in improving metabolic health outcomes.